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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,576	NOGUCHI ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/03/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed July 31, 2008, has been received and entered.

Claims 1-7 are pending in this application and were examined on their merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 3-4 and 6-7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn due to Applicant's amendments to the claims filed on 07/31/208.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koizumi et al. (US 2002/0064836 A1) in view of Plumbridge & Vimr (Journal of Bacteriology, 1999, Vol. 181, No.1. p47-54), and further in view of Tabata et al. (Enzyme & Microbial Technology, March 2002, Vol. 30, p.237-333), and further in view of IUBMB enzyme nomenclature (EC 5.9.3.1).

Claims 1-4 are drawn to a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc), comprises adding yeast cells, N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), N-acetylneuraminic acid lyase (NeuAc lyase), and CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase) to a reaction system containing N-acetylglucosamine (GlcNAc), pyruvate, and cytidine 5'-monophosphate (CMP), and inducing reaction of the mixture.

Claims 5-7 are drawn to a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc), comprises adding yeast cells, N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase), N-acetylneuraminic acid synthase (NeuAc synthase), and CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase) to a reaction system containing N-acetylglucosamine (GlcNAc) and cytidine 5'-monophosphate (CMP), and inducing reaction of the mixture.

Koizumi et al. teach a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc) (p.9 0135), yeast cell can be used to express the gene of interest (page 7 0103), microbial culture broth obtained by the culturing or a treated product of the culture broth obtained by treating the culture broth can be used as a enzyme source (p.8 0122), N-acetylneuraminic acid aldolase (also called

NeuAc lyase), and CMP-N-acetylneuraminic acid synthase (CMP-NeuAc synthase), N-acetylneuraminic acid synthase (NeuAc synthase) (p.5 0089, 0090 and 0091, also page 2 0026, Table 1.), reaction system containing N-acetylglucosamine (GlcNAc), pyruvic acid (or pyruvate)(p.8 0116), and nucleotide precursor used in the formation of sugar nucleotide include cytidine 5'-monophosphate (CMP) (p.9 0135). Koizumi et al. further teach the process is useful for the production of complex carbohydrates useful for protection against infection of bacteria, viruses, and the like, application to cardiovascular disorders and immunotherapy. Koizumi et al. teach using inexpensive nucleotide precursors, sugars, and complex carbohydrate precursors as the starting material in the process (page 1 0001 and 0005, page 13 0185-0197).

Koizumi et al. do not teach N-acetylglucosamine-6-phosphate 2-epimerase (GlcNAc-6P-2-epimerase). However, Plumbridge & Vimr teach enzyme GlcNAc-6P-2-epimerase, the enzyme catalyze the epimerization of N-acetylmannosamine 6-phosphate to N-acetylglucosamine 6-phosphate (ManNAc-6-P-to-GlcNAc-6-P) (see Abstract). Plumbridge & Vimr teach the existence of the putative gene for epimerase function within the *nanAT* operon allows the metabolic pathway for sialic acid to converge with that of ManNAc and GlcNAc at the common intermediate GlcNAc-6-P (p.53 1st column 2nd paragraph). Plumbridge & Vimr further teach 30 yeas ago an enzyme with the function of converting GlcNAc-6-P to ManNAc-6-P was partially purified. Plumbridge & Vimr teach the extracts of strains with YhcJ (gene that encodes the

enzyme) overproduced from a multicopy plasmid have increased capacity to convert GlcNAc-6-P to ManNAc-6-P (p.52 2nd column lines 1-3 and 5-7).

Further motivation is in Tabata et al. who teach NeuAc related compounds have been thought as potential pharmaceuticals and NeuAc analogs were launched as influenza drugs (Introduction 1st column 1st paragraph). Tabata et al. teach because ManNAc is very expensive and not readily available for large-scale production, methods for the preparation of ManNAc from cheap GlcNAc using chemical and enzymatic conversion by Glc-NAc 2-epimerase were developed (Introduction 2nd column 2nd paragraph 7-10 and p.328 1st column 1st paragraph).

Therefore, in view of the above teachings, a person of ordinary skill in the art at the time the invention was made could have been motivated to modify the method of Koizumi et al. by substituting N-acetylglucosamine 2-epimerase with N-acetylglucosamine-6-phosphate 2-epimerase as taught by Plumbridge & Vimr in order to provide a process for producing CMP-N-acetylneuraminic acid (CMP-NeuAc) with predictable results of converting GlcNAc-6-P to ManNAc-6-P. The motivation as taught by Tabata et al. would be the potential of NeuAc related compounds for the development of therapeutics, and to provide an efficient process useful for the production of CMP-NeuAc by using inexpensive precursors (e.g. GlcNAc-6-P) for producing CMP-N-acetylneuraminic acid. The claim method would have been obvious because substitution of one known enzyme, in this case N-acetylglucosamine 2-epimerase with another, in this case

N-acetylglucosamine-6-phosphate 2-epimerase, would yield predictable results to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed on 07/31/2008 with respect to the rejection of claims 1-7 have been fully considered but they are not persuasive.

In response to Applicant arguments that Plumbridge & Vimr GlcNAc-6P-2-epimerase catalyze the reaction ManNAc-6-P to GlcNAc-6P in the metabolic pathway of ManNAc, and this is the reverse reaction to that employed in the claimed invention, and thus the reference fails to teach or suggest GlcNAc-6-P, as mentioned immediately above, GlcNAc-6P-2-epimerase taught by Plumbridge & Vimr, catalyze the epimerization of N-acetylmannosamine 6-phosphate to N-acetylglucosamine 6-phosphate, and a person of ordinary skill in the art would have known that epimerization reaction catalyzed by GlcNAc-6P-2-epimerase is bidirectional. Please see the reaction in IBUMB enzyme nomenclature.

In response to applicant's argument that according to the claimed invention 100nM GlcNAc produced 43.7 mM NeuAc yield 44%. This is significant improvement not taught or suggested by the cited art, it is noted that the features upon which applicant relies (i.e., 44% yield) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, as

mentioned above, Plumbridge & Vimr teach the enzyme can be overproduced from a multicopy plasmid which would increase the capacity to convert GlcNAc-6-P to ManNAc-6-P. Thus, it would have been obvious to obtain higher yield and improve the efficiency of the reaction by increasing the amount and activity of the enzyme in the reaction.

In response to applicant's arguments that Applicant's have shown yeast provide high CMP-NeuAc yield and the claimed invention uses dry yeast to supply CTP, and yeast has the ability to transform CMP to CTP, as mentioned immediately above, Koizumi et al. teach yeast cell can be used to express the gene of interest (page 7 0103), microbial culture broth obtained by the culturing or a treated product of the culture broth obtained by treating the culture broth can be used as a enzyme source (p.8 0122), and adding cytidine 5'-monophosphate (CMP) (p.9 0135). Therefore, Koizumi et al. method could supply CTP from CMP.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory

period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651